REMARKS

Reconsideration and allowance are respectfully requested. The amendments are fully supported by the original disclosure. Thus, no new matter is added by their entry.

Claims 5-11, 14-17 and 19-28 are pending. The claims are limited to mutated HXT3 hexose transporters. The wild-type sequences are SEQ ID NO: 25 (nucleotide sequence) and SEQ ID NO: 26 (amino acid sequence). The claimed nucleic acid has a nucleotide sequence encoding an amino acid sequence derived from SEQ ID NO: 26 and having at least one mutation at position Ile 209. For example, the mutants SEQ ID NOS: 27 and 30 differ from SEQ ID NO: 26 by at least a mutation at position 209 where Ile is replaced by Val. This specific mutation is described on page 5, lines 7-8, and Table 3B of the specification. Specifically, the mutated HXT3 gene I (SEQ ID NO: 28) and the mutated HXT3 gene II (SEQ ID NO: 29) encode amino acid sequences derived from SEQ ID NO: 26 and containing at least the mutation Ile 209 Val. See also page 4, lines 3-18, of the paragraph.

Support for the amendment of claim 5 is found on page 4, lines 3-6, of the specification. In claim 14, the improved capacity to transport involves fructose is based on claim 2 as filed and page 3, lines 10-18, of the specification. Mutating the nucleic acid to encode a mutation at least at position Ile 209 is also supported by claim 18. This limitation is incorporated in independent claims 5 and 14; dependent claim 18 is canceled. Addition of a mutation at position Tyr 389 in claim 17 is supported by page 4, lines 10-15, of the specification; moreover, the specific mutations in claim 19 are supported by page 4, lines 16-18, of the specification. Basis for new claims 20 and 21 is found on page 5, line 7, of the specification.

Claims 5-7, 10, 14-17 and 19-27 are directed to the elected invention. Claims 1-4 and 12-13 were withdrawn from consideration by the Examiner; thus, they are canceled without prejudice to their prosecution in a future application. Note that the species SEQ ID NOS: 28 and 29 belong to the same genus of the elected invention (see claims 5 and 14) because they are both derived from SEQ ID NO: 26 and have at least a mutation at Ile 209. Rejoinder of withdrawn claims 8-9, 11 and 28 is requested upon allowance of

an elected claim because they are directed to processes of making the elected yeast cell and methods of using the elected yeast cell.

Specification Objections

The Examiner objected to the specification. But there is proper antecedent basis for SEQ ID NO: 28. In particular, the specification describes the elected species in paragraph [0015] of the published application:

> The present invention also relates to a new nucleic acid sequence encoding for a HXT3 transporter having an amino acid sequence derived from SEQ ID NO: 26 and having at least one mutation at a position selected from the group consisting of Leu 207, Met 208, Ile 209, Thr 210, Leu 211, Gly 212. Preferably the mutation is selected from the group consisting of Leu 207, Met 208, Ile 209, Thr 210, Leu 211, more preferably selected from the group consisting of Met 208, Ile 209, Thr 210 and most preferably the mutation is positioned at at Ile 209.

Specifically, paragraph [0023] of the published application is amended to state that two examples of the new nucleic acid sequence are SEQ ID NOS: 28 and 29.

The trademark FERMICHAMP® is capitalized in the specification.

Withdrawal of the objections is requested.

35 U.S.C. 112 – Definiteness

Claims 15-19 were rejected under Section 112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

The Examiner required correction of the term "derived" in claim 15. This term is replaced by --obtained or isolated-- because it does not appear to change the scope of the claims and the Examiner indicated the recitation would satisfy her requirement.

Claim 19 is amended to correct the informality noted by the Examiner. A person skilled in the art would understand the genetic nomenclature Ile 209 Val means that the residue isoleucine (Ile) at position 209 is mutated to the residue valine (Val).

The Examiner's suggestion is gratefully acknowledged. Adoption of her suggestion moots the rejection. Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 112 – Enablement

Claim 6 was rejected under Section 112, first paragraph, because it was alleged that the specification "does not reasonably provide enablement for a functional homolog of SEQ ID NO: 28." Applicants traverse because the limitation "functional homologue" is deleted as it is not required for patentability.

Withdrawal of the enablement rejection is requested.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 5, 7, 10, 14 and 16 were rejected under Section 102(b) as allegedly anticipated by Liang et al. (Mol. Cell. Biol. 18:926-935, 1998) as evidenced by Ko et al. (Mol. Cell. Biol. 13:638-648, 1993). Applicants traverse.

Liang discloses a mutation of an HTX3 gene at Gln 206, but no mutation at position Ile 209. But as taught by Applicants on page 5, lines 7-8, of their specification, they surprisingly found even the conservative mutation Ile 209 Val can contribute to a fructophilic phenotype. This discovery was neither taught nor rendered obvious by Liang.

Moreover, Liang is related to glucose transport and would not have been understood to have any relationship to an effect on fructose transport. In particular, the cited document does <u>not</u> teach that a mutation at position 209 (i.e., mutating the wild-type Ile residue) improves fructose transport as compared to the wild type. Instead, Liang would suggest making a mutation at Gln 206 – or another mutation(s) described in the cited document – expecting to see an effect on glucose transport.

Finally, Ko discloses a mutant allele of an HTX3 gene. The gene is deleted by Ko, however, there is no specific position(s) in the HTX3 gene that was mutated. The cited document clearly does not anticipate Applicants' claimed mutated HTX3 gene.

Therefore, Liang does not anticipate Applicants' claimed invention.

Claims 6 and 15 were rejected under Section 102(b) as allegedly anticipated by Contreras et al. (WO 02/64766). Applicants traverse.

Contreras discloses a synthetic BAX gene promoting apoptosis (cell death). It is not identical to SEQ ID NO: 28. In particular, the sequence identity between ABQ76349 of Contreras and SEQ ID NO: 28 is not 100% because of a difference in one nucleotide (see result 4 in the search report by the Examiner). Contreras discloses the triplet 1133-1135 ATT encoding isoleucine, but the corresponding nucleotide sequence in SEQ ID NO: 28 is triplet 625-627 GTT encoding valine. The Examiner's search report shows that there is no match between Contreras' position 1133 and Applicants' position 625 because the vertical bar is missing. Therefore, the cited document discloses the wild-type sequence for an HTX3 gene instead of a mutated HTX3 gene according to Applicants' claimed invention. See paragraph [0015] of the published application: "The present invention also relates to a new nucleic acid sequence encoding for a HXT3 transporter having an amino acid sequence derived from SEQ ID NO: 26 and having at least one mutation . . . . most preferably the mutation is positioned at Ile 209."

This difference of one nucleotide is essential to the surprising improvement achieved by Applicants' invention, which can improve fructose transport and contribute to a fructophilic phenotype. See paragraph [0023] of the published application: "Surprisingly, it was found that even a conservative mutation as Ile 209 Val can contribute to the fructophilic phenotype." This unexpected result was not predicted by the prior art.

Contreras teaches neither SEQ ID NO: 28 nor 29 as the nucleotide sequence, nor any nucleotide sequence of a mutated HTX3 gene. Therefore, the cited document does not anticipate Applicants' claimed invention.

Applicants request withdrawal of the Section 102 rejections.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d

1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). A prima facie case under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn* at 1335; see *KSR* at 1396. An inquiry is required as to "whether the improvement is more than the predictable use of prior art elements according to their established functions.". Id. at 1396. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 14 and 17-19 were rejected under Section 103(a) as allegedly unpatentable over Liang et al. (Mol. Cell. Biol. 18:926-935, 1998). Applicants traverse.

The failure of Liang to disclose the claimed invention (see above) is not remedied by the attempt to modify that disclosure. Among those failures are Liang not teaching or making obvious mutating an HTX3 gene at least at position Ile 209 to improve fructose transport. There is also no reasonable expectation of success in making these modifications. Applicants submit that these features of their claimed invention are sufficient to distinguish over the cited document so any other incorrect allegations about its disclosure are not disputed here, but the opportunity to dispute them in the future is reserved.

All claim limitations must be considered in determining patentability of the claims against the prior art according to M.P.E.P. § 2143.03 and *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970). As noted above, Liang is related to glucose transport and would not have been understood to have any relationship to an effect on fructose transport. In particular, the cited document does not teach that a mutation at position 209 (i.e., mutating the wild-type Ile residue) improves fructose transport as compared to the wild type. Instead, Liang would suggest making a mutation at Gln 206 – or another mutation(s) described in the cited document – expecting to see an effect on glucose transport. It would not have been obvious to modify the HTX3 gene at a different position (i.e., Ile 209) with the objective of improving transport of a different carbohydrate (i.e., fructose).

Therefore, Liang does not make Applicants' claimed invention obvious as viewed by one of ordinary skill in the art when this invention was made.

Applicants request withdrawal of the Section 103 rejection.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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By: _____

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